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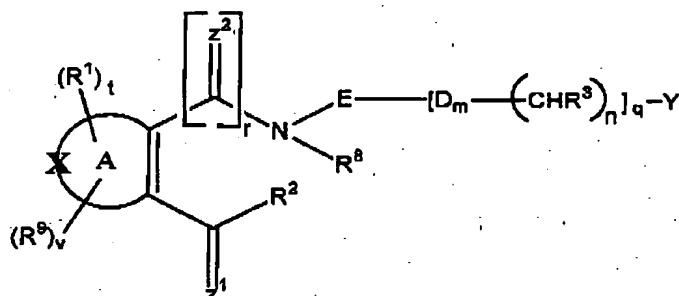
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**CLAIMS:**

1. A compound of the general formula (I) and salts and physiologically functional derivatives thereof.



5

10

wherein

10      A      is a non-aromatic ring system containing 4 to 8 carbon atoms, wherein the ring system comprises at least one double bond and wherein one or more of the carbon atoms in the ring can be replaced by a group X, wherein X is selected from the group consisting of S, O, N, NR<sup>4</sup>, SO, CO or SO<sub>2</sub>;

15      D      is O, S, SO<sub>2</sub>, NR<sup>4</sup> or CH<sub>2</sub>;

15      Z<sup>1</sup> and Z<sup>2</sup> are independent from each other O, S, or NR<sup>5</sup>;

20      R<sup>1</sup>      is independently -CO<sub>2</sub>R'', -SO<sub>3</sub>H, -CONR\*<sup>1</sup>R'', -CR<sup>11</sup>O, -SO<sub>2</sub>-NR\*<sup>1</sup>R'', -NO<sub>2</sub>, -SO<sub>2</sub>-R'', -SO-R<sup>4</sup>, -CN, alkoxy, -OH, -SH, alkylthio, -NR<sup>11</sup>-CO<sub>2</sub>-R', -NR<sup>11</sup>-CO-R<sup>4</sup>, -NR<sup>11</sup>-SO<sub>2</sub>-R', -O-CO-R<sup>4</sup>, -O-CO<sub>2</sub>-R<sup>4</sup>, -O-CO-NR\*<sup>1</sup>R'', cycloalkyl, alkylamino, hydroxyalkylamino, aryl, or heteroaryl;

25      R<sup>9</sup>      is independently H, halogen, haloalkyl, haloalkyloxy or alkyl;

25      R\*<sup>1</sup>      is independently H, alkyl, cycloalkyl, aminoalkyl, alkoxy, -OH, -SH, alkylthio, hydroxyalkyl, haloalkyl, haloalkyloxy, aryl or heteroaryl;

25      R<sup>11</sup>      is independently hydrogen, haloalkyl, hydroxyalkyl, alkyl, cycloalkyl, aryl, heteroaryl or aminoalkyl;

2       $R^2$  is H, OR<sup>6</sup>, or NHR<sup>7</sup>;

5       $R^3$  is H, alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, O-aryl, O-cycloalkyl, halogen, aminoalkyl, alkylamino, hydroxylamino, hydroxylalkyl, haloalkyl, haloalkyloxy, heteroaryl, alkylthio, S-aryl, or S-cycloalkyl;

10      $R^4$  is H, alkyl, cycloalkyl, aryl, or heteroaryl;

15      $R^5$  is H, OH, alkoxy, O-aryl, alkyl, or aryl;

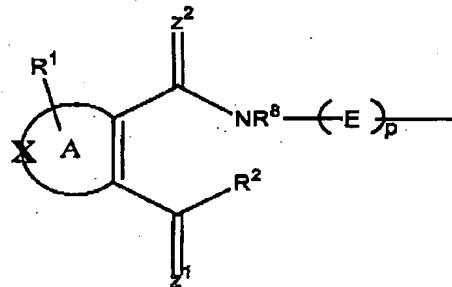
20      $R^6$  is H, alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, alkylaryl, alkoxyalkyl, acylmethyl, (acyloxy)alkyl, non-symmetrical (acyloxy)alkyldiester, or dialkylphosphate;

25      $R^7$  is H, alkyl, aryl, alkoxy, O-aryl, cycloalkyl, or O-cycloalkyl;

$R^8$  is hydrogen or alkyl;

      E is an alkyl or cycloalkyl group or a monocyclic or polycyclic substituted or unsubstituted ring system which may contain one or more groups X and which contains at least one aromatic ring;

      Y is hydrogen, halogen, haloalkyl, haloalkyloxy, alkyl, cycloalkyl, a monocyclic or polycyclic substituted or unsubstituted ring system which may contain one or more groups X and which contains at least one aromatic ring or



m is 0 or 1;

n is 0 or 1;

p is 0 or 1;

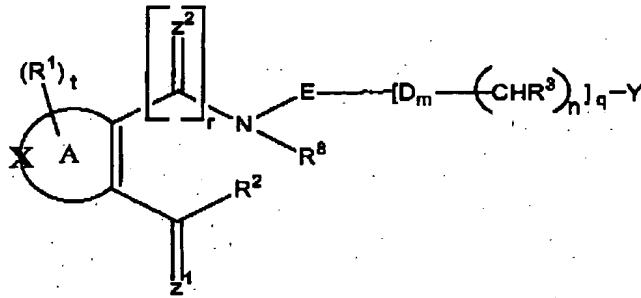
r is 0 or 1;

5 q is 0 or 1;

t is 1 to 3; and

v is 0 to 3;

2. A compound of the general formula (Ia) and salts and physiologically functional  
10 derivatives thereof,



wherein

15 A is a non-aromatic ring system containing 4, 5, 6, 7 or 8 carbon atoms, wherein the ring system comprises at least one double bond and wherein one or more of the carbon atoms in the ring can be replaced by a group X, wherein X is selected from the group consisting of S, O, N, NR<sup>4</sup>, SO, CO or SO<sub>2</sub>;

20 D is O, S, SO<sub>2</sub>, NR<sup>4</sup>, or CH<sub>2</sub>;

Z<sup>1</sup> and Z<sup>2</sup> are independent from each other O, S, or NR<sup>5</sup>;

25 R<sup>1</sup> is independently H, halogen, haloalkyl, haloalkyloxy -CO<sub>2</sub>R<sup>11</sup>, -SO<sub>3</sub>H, -OH, -CONR<sup>4</sup>R<sup>11</sup>, -CR<sup>11</sup>O, -SO<sub>2</sub>-NR<sup>4</sup>R<sup>11</sup>, -NO<sub>2</sub>, -SO<sub>2</sub>-R<sup>11</sup>, -SO-R<sup>4</sup>, -CN, alkoxy, alkylthio, aryl, -NR<sup>4</sup>-CO<sub>2</sub>R<sup>11</sup>, -NR<sup>4</sup>-CO-R<sup>4</sup>, -NR<sup>4</sup>-SO<sub>2</sub>-R<sup>11</sup>, -O-CO-R<sup>4</sup>, -

O-CO<sub>2</sub>-R<sup>4</sup>, -O-CO-NR<sup>5</sup>R<sup>6</sup>; cycloalkyl, alkylamino, hydroxyalkylamino, -SH, heteroaryl, or alkyl;

5 R<sup>4</sup> is independently H, alkyl, cycloalkyl, aminoalkyl, alkoxy, -OH, -SH, alkylthio, hydroxyalkyl, haloalkyl, haloalkyloxy, aryl or heteroaryl;

R<sup>5</sup> is independently hydrogen, haloalkyl, hydroxyalkyl, alkyl, cycloalkyl, aryl, heteroaryl or aminoalkyl;

10 R<sup>2</sup> is NHOH or R<sup>2</sup> together with the nitrogen atom which is attached to R<sup>8</sup> form a 5 or 6 membered heterocyclic ring with the proviso that R<sup>2</sup> is -[CH<sub>2</sub>]<sub>3</sub> and R<sup>8</sup> is absent;

15 R<sup>3</sup> is H, alkyl, cycloalkyl, aryl, alkoxy, O-aryl; O-cycloalkyl, halogen, aminoalkyl, alkylamino, hydroxylamino, hydroxylalkyl, haloalkyloxy, heteroaryl, alkylthio, S-aryl; S-cycloalkyl, arylalkyl, or haloalkyl;

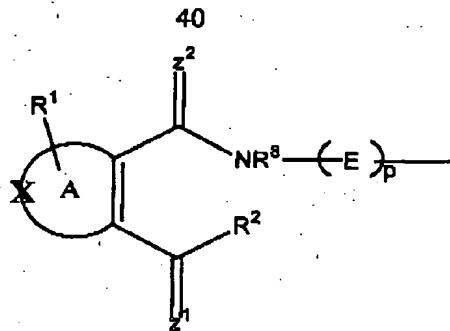
R<sup>4</sup> is H, alkyl, cycloalkyl, aryl or heteroaryl;

R<sup>5</sup> is H, OH, alkoxy, O-aryl, alkyl or aryl;

20 R<sup>8</sup> is hydrogen, or alkyl;

E is an alkyl or cycloalkyl group or a monocyclic or polycyclic substituted or unsubstituted ring system which may contain one or more groups X and which contains at least one aromatic ring;

25 Y is hydrogen, halogen, haloalkyl, haloalkyloxy, alkyl, cycloalkyl, a monocyclic or polycyclic substituted or unsubstituted ring system which may contain one or more groups X and which contains at least one aromatic ring or



- $m$  is 0 or 1;
- $n$  is 0 or 1;
- $p$  is 0 or 1;
- $r$  is 0 or 1;
- $q$  is 0 or 1;
- $s$  is 0 to 2; and
- $t$  is 0 to 3;

10

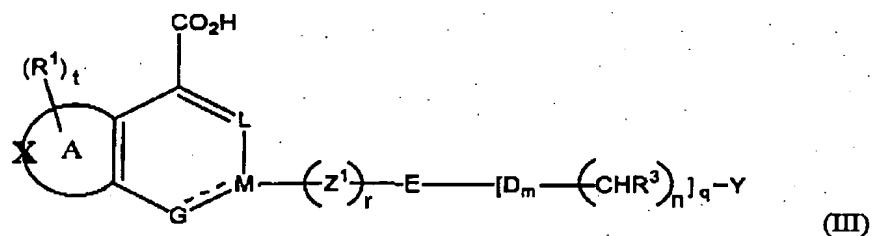
with the proviso that the following compounds are excluded:

15 compounds wherein ring A is an unsubstituted carbocycle containing six carbon atoms and one double bond between the  $CZ^1$  and  $CZ^2$ -substituents,  $Z^1=Z^2=O$ , and s is 0; 1,3,5-Tribenzyl-2,4,6-trioxopyrrolo[3,4-d]imidazole, 1,3-Dibenzyl-5-(4-methoxy-benzyl)-2,4,6-trioxopyrrolo[3,4-d]imidazole, 1,3-Bis-(4-methoxybenzyl)-5-benzyl-2,4,6-trioxopyrrolo[3,4-d]imidazole, and 1,3-Tris-(4-methoxybenzyl)-2,4,6-trioxo-pyrrolo[3,4-d]imidazole.

15

20 3. A compound of the general formula (III) and salts and physiologically functional derivatives thereof,

20



wherein

the dotted line means a single or a double bond;

5           A       is a non-aromatic ring system containing 4, 5, 6, 7 or 8 carbon atoms, wherein the ring system comprises at least one double bond and wherein one or more of the carbon atoms in the ring can be replaced by a group X, wherein X is selected from the group consisting of S, O, N, NR<sup>4</sup>, SO, CO or SO<sub>2</sub>;

10           D       is O, S, SO<sub>2</sub>, NR<sup>4</sup>, or CH<sub>2</sub>;

15           G       is O, S, SO<sub>2</sub>, CO, N, NR<sup>4</sup>, CR<sup>1</sup> or CHR<sup>1</sup>;

20           L       is N or CR<sup>1</sup>;

25           M       is N or CR<sup>5</sup>;

30           Z<sup>1</sup>      is O, S, or NR<sup>5</sup>; NR<sup>4</sup>CONR<sup>4</sup>, CONR<sup>4</sup>, or CO;

35           R<sup>1</sup>      is independently H, halogen, haloalkyl, haloalkyloxy -CO<sub>2</sub>R'', -SO<sub>3</sub>H, -OH, -CONR<sup>4</sup>R'', -CR<sup>1</sup>O, -SO<sub>2</sub>-NR<sup>4</sup>R'', -NO<sub>2</sub>, -SO<sub>2</sub>-R'', -SO-R\*, -CN, alkoxy, alkylthio, aryl, -NR<sup>4</sup>-CO<sub>2</sub>R', -NR<sup>4</sup>-CO-R\*, -NR<sup>4</sup>-SO<sub>2</sub>-R', -O-CO-R\*, -O-CO<sub>2</sub>-R\*, -O-CO-NR<sup>4</sup>R'', cycloalkyl, alkylamino, hydroxyalkylamino, -SH, heteroaryl, or alkyl;

40           R\*      is independently H, alkyl, cycloalkyl, aminoalkyl, alkoxy, -OH, -SH, alkylthio, hydroxyalkyl, haloalkyl, haloalkyloxy, aryl or heteroaryl;

45           R''     is independently hydrogen, haloalkyl, hydroxyalkyl, alkyl, cycloalkyl, aryl, heteroaryl or aminoalkyl;

50           R<sup>3</sup>      is H, alkyl, cycloalkyl, aryl, alkoxy, O-aryl; O-cycloalkyl, halogen, aminoalkyl, alkylamino, hydroxylamino, hydroxylalkyl, haloalkyloxy, heteroaryl, alkylthio, S-aryl; S-cycloalkyl, arylalkyl, or haloalkyl;

55           R<sup>4</sup>      is H, alkyl, cycloalkyl, aryl or heteroaryl;

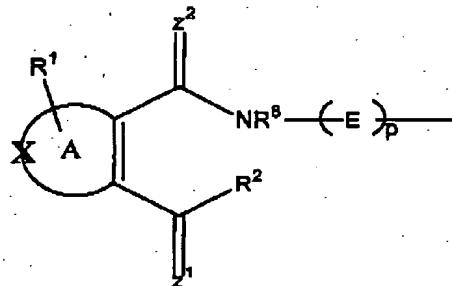
5            R<sup>5</sup>      is H, OH, alkoxy, O-aryl, alkyl or aryl;

5            R<sup>7</sup>      is H, OH, alkyl, aryl, alkoxy, O-aryl, cycloalkyl, or O-cycloalkyl;

10            R<sup>8</sup>      is hydrogen, or alkyl;

10            E      is an alkyl or cycloalkyl group or a monocyclic or polycyclic substituted or unsubstituted ring system which may contain one or more groups X and which contains at least one aromatic ring;

15            Y      is hydrogen, halogen, haloalkyl, haloalkyloxy, alkyl, cycloalkyl, a monocyclic or polycyclic substituted or unsubstituted ring system which may contain one or more groups X and which contains at least one aromatic ring or



20            m      is 0 or 1;

              n      is 0 or 1;

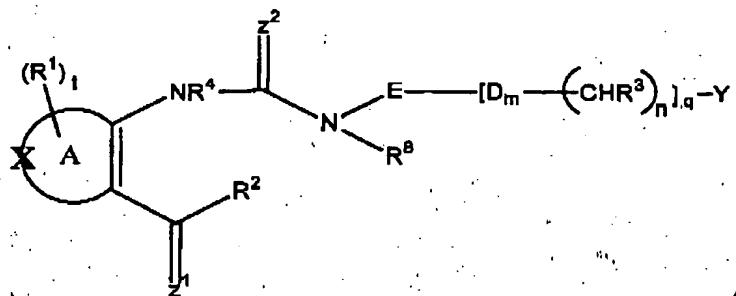
              p      is 0 or 1;

              r      is 0 or 1;

              q      is 0 or 1; and

              t      is 0 to 3;

25            4.      A compound of the general formula (IV) and salts and physiologically functional derivatives thereof,



(IV)

wherein

5        A        is a non-aromatic ring system containing 4, 5, 6, 7 or 8 carbon atoms, wherein the ring system comprises at least one double bond and wherein one or more of the carbon atoms in the ring can be replaced by a group X, wherein X is selected from the group consisting of S, O, N, NR<sup>4</sup>, SO, CO or SO<sub>2</sub>;

10      D        is O, S, SO<sub>2</sub>, NR<sup>4</sup>, or CH<sub>2</sub>;

Z<sup>1</sup> and Z<sup>2</sup> are independent from each other O, S, or NR<sup>5</sup>;

15      R<sup>1</sup>      is independently H, halogen, haloalkyl, haloalkyloxy -CO<sub>2</sub>R'', -SO<sub>3</sub>H, -OH, -CONR\*R'', -CR''O, -SO<sub>2</sub>-NR\*<sup>2</sup>R'', -NO<sub>2</sub>, -SO<sub>2</sub>-R'', -SO-R\*, -CN, alkoxy, alkylthio, aryl, -NR''-CO<sub>2</sub>-R', -NR''-CO-R\*, -NR''-SO<sub>2</sub>-R', -O-CO-R\*, -O-CO<sub>2</sub>-R\*, -O-CO-NR\*<sup>2</sup>R''; cycloalkyl, alkylamino, hydroxyalkylamino, heteroaryl, -SH, or alkyl;

20      R\*      is independently H, alkyl, cycloalkyl, aminoalkyl, alkoxy, -OH, -SH, alkylthio, hydroxyalkyl, haloalkyl, haloalkyloxy, aryl or heteroaryl;

R''      is independently hydrogen, haloalkyl, hydroxyalkyl, alkyl, cycloalkyl, aryl, heteroaryl or aminoalkyl;

25      R<sup>2</sup>      is H or OR<sup>6</sup>, NHR<sup>7</sup>, NR<sup>7</sup>OR<sup>7</sup> or R<sup>2</sup> together with the nitrogen atom which is attached to R<sup>8</sup> form a 6 membered heterocyclic ring with the proviso that R<sup>2</sup> is -[CH<sub>2</sub>]<sub>2</sub> and R<sup>8</sup> is absent;

5            R<sup>3</sup>    is H, alkyl, cycloalkyl, aryl, alkoxy, O-aryl, O-cycloalkyl, halogen, aminoalkyl, alkylamino, hydroxylamino, hydroxylalkyl, haloalkyloxy, heteroaryl, alkylthio, S-aryl; S-cycloalkyl, arylalkyl, or haloalkyl;

10            R<sup>4</sup>    is H, alkyl, cycloalkyl, aryl or heteroaryl;

15            R<sup>5</sup>    is H, OH, alkoxy, O-aryl, alkyl or aryl;

20            R<sup>6</sup>    is H, alkyl, cycloalkyl, aryl, arylalkyl, heteroaryl, alkylaryl, alkoxyalkyl, acylmethyl, (acyloxy)alkyl, non-symmetrical (acyloxy)alkyldiester, or dialkylphosphate;

25            R<sup>7</sup>    is H, OH, alkyl, aryl, alkoxy, O-aryl, cycloalkyl, or O-cycloalkyl;

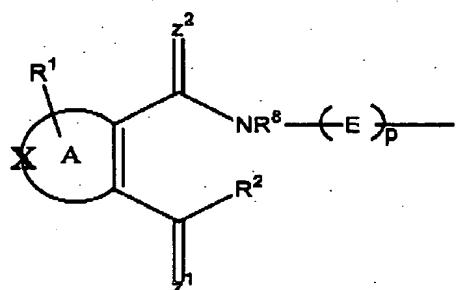
30            R<sup>8</sup>    is hydrogen, or alkyl;

35            E    is an alkyl or cycloalkyl group or a monocyclic or polycyclic substituted or unsubstituted ring system which may contain one or more groups X and which contains at least one aromatic ring;

40            Y    is hydrogen, halogen, haloalkyl, haloalkyloxy, alkyl, cycloalkyl, a monocyclic or polycyclic substituted or unsubstituted ring system which may contain one or more groups X and which contains at least one aromatic ring or

45            m    is 0 or 1;

50            n    is 0 or 1;



p      is 0 or 1;  
 q      is 0 or 1;  
 s      is 0 to 2; and  
 t      is 0 to 3;

5

with the proviso that the following compounds are excluded:

5,5-Dimethyl-4-phenyl-2-(3-phenyl-ureido)-4,5-dihydro-furan-3-carboxylic acid  
 methyl ester, 2[3-(4-Chlorophenyl-ureido)]-5,5-dimethyl-4-phenyl-4,5-dihydro-  
 furan-3-carboxylic acid methyl ester, 2[3-(4-Methoxyphenyl-ureido)]-5,5-  
 10      dimethyl-4-phenyl-4,5-dihydro-furan-3-carboxylic acid methyl ester, 2[3-(4-  
 Methylphenyl-ureido)]-5,5-dimethyl-4-phenyl-4,5-dihydro-furan-3-carboxylic acid  
 methyl ester, 2[3-(4-Nitrophenyl-ureido)]-5,5-dimethyl-4-phenyl-4,5-dihydro-  
 furan-3-carboxylic acid methyl ester, 4-(4-Chlorophenyl)-5,5-dimethyl-2-(3-  
 phenyl-ureido)-4,5-dihydro-furan-3-carboxylic acid methyl ester, 4-(4-  
 15      Chlorophenyl)-2[3-(4-chlorophenyl-ureido)]-5,5-dimethyl-4,5-dihydro-furan-3-  
 carboxylic acid methyl ester, 4-(4-Chlorophenyl)-2[3-(4-methoxyphenyl-ureido)]-  
 5,5-dimethyl-4,5-dihydro-furan-3-carboxylic acid methyl ester, 4-(4-  
 Chlorophenyl)-2[3-(4-methylphenyl-ureido)]-5,5-dimethyl-4,5-dihydro-furan-3-  
 carboxylic acid methyl ester, or 4-(4-Chlorophenyl)-2[3-(4-nitrophenyl-ureido)]-  
 20      5,5-dimethyl-4,5-dihydro-furan-3-carboxylic acid methyl ester.

5.      A pharmaceutical composition comprising a compound as defined in claim 1 in free  
 form or in the form of a pharmaceutically acceptable salt or physiologically  
 functional derivative and a pharmaceutically acceptable diluent or carrier.

25      6.      A compound according to claim 1 for the use as a medicament.

7.      A method for the treatment of a disease or a therapeutic indication in which  
 inhibition of dihydroorotate dehydrogenase is beneficial comprising administering  
 30      to a mammal an effective amount of a compound as defined in claim 1 or a  
 physiologically functional derivative or a pharmacologically tolerable salt thereof.

8.      A method for the treatment of a disease or a therapeutic indication in which  
 inhibition of dihydroorotate dehydrogenase is beneficial comprising administering  
 35      to a mammal an effective amount of a compound as defined in claim 2, including

the compounds excluded in claim 2, or a physiologically functional derivative or pharmacologically tolerable salt thereof.

9. A method for the treatment of a disease or a therapeutic indication in which inhibition of dihydroorotate dehydrogenase is beneficial comprising administering to a mammal an effective amount of a compound as defined in claim 3 or a physiologically functional derivative or a pharmacologically tolerable salt thereof.
- 5 10. A method for the treatment of a disease or a therapeutic indication in which inhibition of dihydroorotate dehydrogenase is beneficial comprising administering to a mammal an effective amount of a compound as defined in claim 4, including the compounds excluded in claim 4, and a physiologically functional derivative or a pharmacologically tolerable salt thereof.
- 10 15. 11. A method for the treatment of a disease or a therapeutic indication selected from the group consisting of rheumatism, acute immunological disorders, autoimmune diseases, diseases caused by malignant cell proliferation, inflammatory diseases, diseases that are caused by protozoal infestations in humans and animals, diseases that are caused by viral infections and *Pneumocystis carinii*, fibrosis, uveitis, rhinitis, asthma and arthropathy comprising administering to a mammal an effective amount of a compound as defined in claim 1 or a physiologically functional derivative or a pharmacologically tolerable salt thereof.
- 20 25. 12. A method for the treatment of a disease or a therapeutic indication selected from the group consisting of rheumatism, acute immunological disorders, autoimmune diseases, diseases caused by malignant cell proliferation, inflammatory diseases, diseases that are caused by protozoal infestations in humans and animals, diseases that are caused by viral infections and *Pneumocystis carinii*, fibrosis, uveitis, rhinitis, asthma and arthropathy comprising administering to a mammal an effective amount of a compound as defined in claim 2, including the compounds excluded in claim 2, or a physiologically functional derivative or pharmacologically tolerable salt thereof.
- 30

13. A method for the treatment of a disease or a therapeutic indication selected from the group consisting of rheumatism, acute immunological disorders, autoimmune diseases, diseases caused by malignant cell proliferation, inflammatory diseases, diseases that are caused by protozoal infestations in humans and animals, diseases that are caused by viral infections and *Pneumocystis carinii*, fibrosis, uveitis, rhinitis, asthma and atropathy comprising administering to a mammal an effective amount of a compound as defined in claim 3 or a physiologically functional derivative or a pharmacologically tolerable salt thereof.

10 14. A method for the treatment of a disease or a therapeutic indication selected from the group consisting of rheumatism, acute immunological disorders, autoimmune diseases, diseases caused by malignant cell proliferation, inflammatory diseases, diseases that are caused by protozoal infestations in humans and animals, diseases that are caused by viral infections and *Pneumocystis carinii*, fibrosis, uveitis, rhinitis, asthma and atropathy comprising administering to a mammal an effective amount of a compound as defined in claim 4, including the compounds excluded in claim 4, and a physiologically functional derivative or a pharmacologically tolerable salt thereof.

15

20 15. The use of a compound according to claim 1 for the inhibition of DHODH.

16. The use of a compound according to claim 2 for the inhibition of DHODH.

17. The use of a compound according to claim 3 for the inhibition of DHODH.

25 18. The use of a compound according to claim 4 for the inhibition of DHODH.